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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,701	01/05/2001	Allan S. Hoffman	UWOTL119001	3998
26389 7590 08/09/2007 CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC 1420 FIFTH AVENUE SUITE 2800 SEATTLE, WA 98101-2347			EXAMINER EPPERSON, JON D	
			ART UNIT 1639	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

**Application No.**

09/755,701

**Applicant(s)**

HOFFMAN ET AL.

**Examiner**

Jon D. Epperson

**Art Unit**

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 03 May 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 3,4,8,9,13-17,19,34-36 and 38-47 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3,4,8,9,13-17,19,34-36, and 38-47 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of the Application***

1. The Response filed May 3, 2007 is acknowledged.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

### ***Status of the Claims***

3. Claims 3, 4, 8, 9, 13-17, 19, 34-36, and 38-44 were pending. Claims 45-47 were added and claims 4, 36, 38 and 41 were amended. Therefore, claims 3, 4, 8, 9, 13-17, 19, 34-36, and 38-47 are currently pending and examined on the merits.

### **Withdrawn Objections/Rejections**

4. The Vinogradov et al. rejection is withdrawn in view of Applicants' amendments adding the "vinyl type" limitation. Rejections of claims over prior art should not be based on speculation as to the meaning of terms employed and assumptions as to the scope of the claims. *In re Steele*, 305 F.2d 859, 862, 134 USPQ 292, 295 (CCPA 1962). The Nair et al. rejection (5,078,994) under 102/103 is withdrawn in view of Applicants' amendments adding the water-soluble limitation. All other rejections are maintained and the arguments are addressed below.

### **Outstanding Objections and/or Rejections**

#### ***Claim Rejections - 35 USC § 112***

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5. Claims 3, 4, 8, 9, 13-17, 19, 34-36, and 38-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A-C. For *claims 36, 38, 39, 41*, use of the term “vinyl type” is vague and indefinite. The addition of the word “type” to an otherwise definite expression (i.e., vinyl) extends the scope of the expression so as to render it indefinite. See *Ex parte Copenhaver*, 109 USPQ 118 (Bd. App. 1955). See also MPEP § 2173.05(b). Therefore, claim 36, 38, 39, 41 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

### ***Response***

6. Applicant’s arguments directed to the above 35 U.S.C. 112, second paragraph rejections were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from its original version to more clearly address applicants’ newly amended and/or added claims and/or newly amended arguments.

A. [1] Applicants argue, “Applicants have cited several publications that report vinyl-type polymers ... The term ‘vinyl-type’ is widely used in the field of polymers” (e.g., see 1/23/07 Response, pages 7 and 8, especially page 8, last two paragraphs).

[2] Applicants argue, “A search in the Lexis database ... reveals that there are 580 issued U.S. patents that include the term ‘vinyl type polymer’ ... [Thus,] [t]he Examiner’s rejection ... is inconsistent with the established position by the U.S. Patent and Trademark Office” (e.g., see 1/23/07 Response, pages 8 and 9).

This is not found persuasive for the following reasons:

[1] The Examiner respectfully disagrees. This argument was found to be non-persuasive in *Ex parte Copenhagen* because, according to the Court, “scientific publications ... are not subject to the rigid legal requirements for definiteness that apply to patent claims.” See *Ex parte Copenhagen*, 109 USPQ 118 (Bd. App. 1955).

[2] The Court also addressed this point head on in *Ex parte Copenhagen* stating, “The fact that the expression may have been used in claims of certain patents likewise does not alter our view on the question [i.e., that the use of the word ‘type’ to an otherwise definite expression extends the scope to render it objectionable under 35 U.S.C. § 112, second paragraph].” See *Ex part Copenhagen*, 109 USPQ 118 (Bd. App. 1955).

Accordingly, the 35 U.S.C. 112, second paragraph rejections cited above are hereby maintained.

### **New Rejections**

#### ***Claims Rejections - 35 U.S.C. 102/103***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

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such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
8. Claims 3, 4, 8, 9, 13-15, 34-36, 38, 40, 41, and 43-47 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Davaran et al. (Davaran et al., "Hydrophilic copolymers prepared from acrylic type derivatives of ibuprofen containing hydrolyzable thioester bond" *Eur. Polym. J.* **1998**, 34(2), 187-192) as evidenced by Applicants' specification and Baroni et al. (Baroni et al., "Effect of ibuprofen and warfarin on the allosteric properties of haem-human serum albumin" *Eur. J. Biochem.* **2001**, 268, 6214-6220).

For **claim 3**, Davaran et al. teach the composition of claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is an organic molecule (e.g., see abstract wherein ibuprofen is disclosed).

For **claim 4**, Davaran et al. teach the composition of claim 36, wherein the hydrophobic component is a synthetic vinyl-type hydrophobic polymer, naturally derived polymer, a membrane disruptive peptide, or a phospholipid bilayer disrupting agent (e.g.,

see page 189, scheme 2 disclosing methacrylate “vinyl-type” polymer).

For **claims 8 and 40**, Davaran et al. teach the composition of claims 36 or 38, wherein the pH-sensitive linkage is an ester (e.g. see Davaran et al., page 190, column 2, paragraph 2 wherein PEG is connected to the methacrylate via an ester linkage).

For **claim 9**, Davaran et al. teach the composition of claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is coupled to either the hydrophilic or the hydrophobic component by a degradable or disruptable linkage (e.g., see abstract wherein ibuprofen is connected via a hydrolysable thioester linkage; see also figures 1-3 showing hydrolysis rates).

For **claim 13**, Davaran et al. teach the composition of claim 36, wherein the conjugate further comprises a ligand, wherein the ligand specifically binds to a target molecule (e.g., see abstract wherein ibuprofen is disclosed). Davaran et al. do not explicitly state that ibuprofen is a ligand for a target but the Examiner contends that this is an inherent property of ibuprofen as exemplified by Baroni (e.g., see Baroni et al., page 6215, column 2, first full paragraph, “Ibuprofen binds to Sudlow’s site II [on HSA] with  $K_d = 3.7 \times 10^{-7} \text{ M}$ ”).

For **claim 14**, Davaran et al. teach the composition of claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is complexed to a component of the conjugate (e.g., see scheme 2 and experimental).

For **claim 15**, Davaran et al. do not explicitly teach the composition of claim 36, wherein the pH sensitive linkage is hydrolyzed within about 30 to 60 minutes at a pH between 5.0 and 5.5. However, Davaran et al. discloses Applicants’ preferred ester

linkage and, as a result, the Examiner contends that this would be an inherent property of the conjugate (e.g., see arguments for claim 36 below).

For **claim 34**, Davaran et al. teach the composition of claim 36 further comprising an agent, wherein the agent is a therapeutic, diagnostic, or prophylactic agent (e.g., see page 189, column 2, wherein a therapeutic drug is disclosed; see also abstract wherein ibuprofen is disclosed).

For **claim 35**, Davaran et al. teach the composition of claim 36, wherein the hydrophobic component comprises a synthetic polymer (e.g., see Davaran et al., page 189, scheme 2).

For **claim 36**, Davaran et al. teach hydrophilic copolymers prepared from acrylic type derivatives of ibuprofen containing hydrolysable thioester bonds (e.g., see Davaran et al., title and abstract), which anticipates the claimed invention. For example, Davaran et al. teach a water-soluble hydrophilic conjugate having a hydrophobic component linked to a hydrophilic component by a pH-sensitive linkage (e.g., see Davaran et al., page 189, scheme 2 showing conjugate with methacrylate hydrophobic component; see also page 190, column 2, paragraph 2 wherein the water-soluble PEG is linked via a pH sensitive ester bond to the methacrylate). Please note that Davaran et al. do not explicitly state that the ester bond in the PEGM is a pH-sensitive linkage that is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 but the Examiner contends that this is an inherent feature of the ester bond as exemplified by Applicants' specification (e.g., see specification, pages 22 and 23, especially page 23, first full paragraph disclosing ester as a "preferred" linkage with these properties; see also page 25, lines 9

and 10, “an ester or acetal bond, which is disrupted upon exposure to a stimulus, for example, a change in pH”). When the reference discloses all the limitations of a claim except a property or function, and the examiner cannot determine whether or not the reference inherently possesses properties which anticipate or render obvious the claimed invention, “[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency’ under 35 U.S.C. 102, on prima facie obviousness’ under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted].” The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980) (a case indicating that the burden of proof can be shifted to the applicant to show that the subject matter of the prior art does not possess the characteristic relied on whether the rejection is based on inherency under 35 U.S.C. § 102 or obviousness under 35 U.S.C. § 103). See MPEP §§ 2112- 2112.02. In addition, cleaving the conjugate at this ester bond would release the hydrophobic component (i.e., the acrylic “vinyl type” polymer) from the hydrophilic component (i.e., the PEG). Davaran et al. do not explicitly state that the hydrophobic component will disrupt a membrane when released from the hydrophilic conjugate but the Examiner contends that this is intended use language and thus should not be afforded any patentable weight or, alternatively, is inherently disclosed by the reference since the hydrophobic polymer possesses the same “vinyl type” methacrylate structure as that currently claimed by Applicants (e.g., see claims 39, 46, and 47; see especially page 11, lines 24 and 25, “Random, block and graft copolymers that include

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acrylate groups and alkyl substituted acrylate groups are preferred.”). “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). See also MPEP § 2112-2112.02.

For **claim 38**, Davaran et al. teach a water-soluble conjugate comprising (a) a hydrophobic synthetic vinyl-type polymer (e.g., see Davaran et al., page 189, showing methacrylate polymer; see also page 190, column 2, paragraph 2 disclosing use of water-soluble PEGM). Davaran et al. do not explicitly state that the polymer is an endosomal membrane disruptive when released from the hydrophilic conjugate but the Examiner contends that this is intended use language and thus should not be afforded any patentable weight or, alternatively, is inherently disclosed by the reference since the hydrophobic polymer possesses the same “vinyl type” methacrylate structure as that currently claimed by Applicants (e.g., see claims 39, 46, and 47; see especially page 11, lines 24 and 25, “Random, block and graft copolymers that include acrylate groups and alkyl substituted acrylate groups are preferred.”). “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and

the burden is on the applicants to establish the difference. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). See also MPEP § 2112-2112.02. Davaran et al. also disclose **(b)** a plurality of pendant hydrophilic polyalkylene oxide components (e.g., see scheme 2 and page 190, column 2, paragraph 2 wherein a plurality of PEGs are incorporated into the conjugate via the PEGMs). Finally, Davaran et al. disclose **(c)** a plurality of pH-sensitive linkages (e.g., see scheme and page 190, column 2, paragraph 2 wherein the plurality of PEGs are attached via an ester linkage). Again, Davaran et al. do not explicitly state that each of the pendant polyalkylene oxide components are covalently linked to the polymer through a pH-sensitive linkage that is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5. However, the Examiner contends that this is an inherent feature of the ester bond as exemplified by Applicants' specification (e.g., see specification, pages 22 and 23, especially page 23, first full paragraph disclosing ester as a "preferred" linkage with these properties; see also page 25, lines 9 and 10, "an ester or acetal bond, which is disrupted upon exposure to a stimulus, for example, a change in pH"). When the reference discloses all the limitations of a claim except a property or function, and the examiner cannot determine whether or not the reference inherently possesses properties which anticipate or render obvious the claimed invention, "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden

of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980) (a case indicating that the burden of proof can be shifted to the applicant to show that the subject matter of the prior art does not possess the characteristic relied on whether the rejection is based on inherency under 35 U.S.C. § 102 or obviousness under 35 U.S.C. § 103). See MPEP §§ 2112-2112.02.

For **claim 41**, Davaran et al. teach in addition to the limitations set forth in claim 38 use of a therapeutic or diagnostic agent such as ibuprofen (e.g., see Davaran et al., abstract).

For **claim 43**, Davaran et al. teach the composition of claim 41, wherein the pH-sensitive linkage is selected from the group consisting of ... an ester (e.g., see Davaran et al., page 190, column 2, paragraph 2 wherein PEG is connected to the methacrylate via an ester linkage).

For **claim 44**, Davaran et al. teach the composition of claim 41, wherein the therapeutic or diagnostic agent is selected from the group consisting of a protein ... an organic molecule (e.g., see abstract wherein ibuprofen is disclosed).

For **claim 45**, Davaran et al. teach the composition of claim 36, wherein the hydrophobic component comprises a random, block, or graft copolymer, wherein the copolymer comprises an alkyl substituted or unsubstituted acrylate group (e.g., see scheme 2 wherein methacrylate is disclosed).

For **claim 46**, Davaran et al. teach the composition of claim 36, wherein the hydrophobic component comprises poly(ethylacrylic acid), poly(propylacrylic acid),

poly(butylacrylic acid), or acrylic acid polymer and copolymers (e.g., see scheme 2 wherein methacrylate is disclosed).

For **claim 47**, Davaran et al. teach a composition for enhancing transport through a membrane, comprising a hydrophilic conjugate having a hydrophobic component linked to a hydrophilic component by a pH-sensitive linkage (e.g., see scheme 2 and page 190, column 2, paragraph 1 wherein a hydrophobic methacrylate polymer is linked via a pH-sensitive linkage to a hydrophilic PEG). Davaran et al. do not explicitly state that the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component, but the Examiner contends that this is an inherent feature of the ester bond as exemplified by Applicants' specification (e.g., see specification, pages 22 and 23, especially page 23, first full paragraph disclosing ester as a "preferred" linkage with these properties; see also page 25, lines 9 and 10, "an ester or acetal bond, which is disrupted upon exposure to a stimulus, for example, a change in pH"). When the reference discloses all the limitations of a claim except a property or function, and the examiner cannot determine whether or not the reference inherently possesses properties which anticipate or render obvious the claimed invention, "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980) (a case

indicating that the burden of proof can be shifted to the applicant to show that the subject matter of the prior art does not possess the characteristic relied on whether the rejection is based on inherency under 35 U.S.C. § 102 or obviousness under 35 U.S.C. § 103). See MPEP §§ 2112- 2112.02. In addition, Davaran et al. disclose a hydrophilic component comprises a polyalkylene oxide (e.g., PEG, see above) and a hydrophobic component comprises a random, block, or graft copolymer, wherein the copolymer comprises an alkyl substituted or unsubstituted acrylate group (e.g., see scheme 2, wherein methacrylate polymer is disclosed). Finally, Davaran et al. do not explicitly state that the hydrophobic component is membrane disruptive and allows enhanced transport through a membrane when released from the hydrophilic conjugate but the Examiner contends again that this is intended use language and thus should not be afforded any patentable weight or, alternatively, is inherently disclosed by the reference since the hydrophobic polymer possesses the same “vinyl type” methacrylate structure as that currently claimed by Applicants (e.g., see claims 39, 46, and 47; see especially page 11, lines 24 and 25, “Random, block and graft copolymers that include acrylate groups and alkyl substituted acrylate groups are preferred.”). “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). See also MPEP § 2112-2112.02.

***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 3, 4, 8, 9, 13-17, 19, 34-36, 38, 40, 41, 43-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davaran et al. (Davaran et al., "Hydrophilic copolymers prepared from acrylic type derivatives of ibuprofen containing hydrolyzable thioester bond" *Eur. Polym. J.* **1998**, 34(2), 187-192) in view of Arnold (U.S. Patent No. 4,571,400) (Date of Patent is **Feb. 18, 1986**) and Vinogradov et al. (Vinogradov et al., "Self-Assembly of Polyamine-Poly(ethylene glycol) Copolymers with Phosphorothioate Oligonucleotides" *Bioconjugate Chem.* **1998**, 9, 805-812) (of record) as evidenced by Applicants' specification and Baroni et al. (Baroni et al.,

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“Effect of ibuprofen and warfarin on the allosteric properties of haem-human serum albumin”

*Eur. J. Biochem.* **2001**, 268, 6214-6220).

For **claims 3, 4, 8, 9, 13-15, 34-36, 38, 40, 41, and 43-47**, Davaran et al. teach all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates and, as a result, renders obvious claims 3, 4, 8, 9, 13-15, 34-36, 38, 40, 41, and 43-47. *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983) (“anticipation is the epitome of obviousness”); see also *In re Skoner*, 517 F.2d 947, 950, 186 USPQ 80, 83 (CCPA 1975); *In re Pearson*, 494 F.2d 1399, 1402, 181 USPQ 641, 644 (CCPA 1974).

The prior art teaching of Davaran et al. differ from the claimed invention as follows:

For **claims 16 and 17**, Davaran et al. fail to teach the composition of claim 36 further comprising a pharmaceutically acceptable carrier for delivery of the conjugate to a cell or organelle.

For **claim 19**, Davaran et al. fail to teach the composition of claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is an antisense nucleotide, ribozyme, ribozyme guide sequence, triplex forming oligonucleotide, or gene.

However, Arnold teaches the following limitations that are deficient in Davaran et al.:

For **claims 16 and 17**, Arnold (see entire document) teaches the use of a wide range of pharmaceutically acceptable carriers for use with ibuprofen (e.g., see Arnold, column 3, lines 1-55), which would encompass the ibuprofen disclosed by Davaran.

For *claim 19*, Vinogradov et al. teach the composition of claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is, for example, an antisense nucleotide (e.g., see page 807, right col., line 8 thru page 808, right col., line 23; see also page 806, left col., lines 44-65).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention to use a pharmaceutically acceptable carrier with the ibuprofen complex disclosed by Davaran et al. because Arnold explicitly state that pharmaceutical carriers can be used in conjunction with ibuprofen (e.g., see Arnold, column 3, lines 1-55; see also claims 4 and 6). A person of ordinary skill in the art would have been motivated to use a pharmaceutically acceptable carrier because Arnold teach that these carriers are useful for administering the drug to a mammal and claim it as a “preferred” embodiment (e.g., see Arnold, column 3, lines 1-55; see also claims 4 and 6). Finally, a person of ordinary skill in the art would reasonably have expected be successful because the use of pharmaceutically acceptable carriers is well known and Arnold explicitly state that it can be used in conjunction with ibuprofen, which would encompass the ibuprofen disclosed by Davaran.

In addition, it would have *been prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the antisense oligonucleotides as disclosed by Vinogradov et al. for the ibuprofen as disclosed by Davaran et al. because Davaran et al. teach that any therapeutic molecule can be attached to their hydrophilic copolymers (e.g., see Davaran et al., Introduction), which would encompass the antisense oligonucleotides disclosed by Viogradov et al. Furthermore, a person of ordinary skill in

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the art would have been motivated to use the hydrophilic copolymers to prevent degradation of the oligonucleotides and/or side effects (e.g., see Davaran et al., Introduction). Furthermore, a person of ordinary skill in the art would reasonably have expected to be successful because Vinogradov et al. teach that the anti-sense oligonucleotides can be conjugated to PEG polymers like the PEG polymer disclosed by Davaran.

### ***Conclusion***

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.  
July 22, 2007

JON EPPERSON  
PRIMARY EXAMINER

